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# Diagnostic value of the pulmonary vein-to-right pulmonary artery ratio in dogs with pulmonary hypertension of precapillary origin☆,☆☆

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**Abstract** *Introduction:* Non-invasive diagnosis of pulmonary hypertension (PH) relies on estimation of pulmonary arterial pressure (PAP) via Doppler echocardiographic measurement of tricuspid regurgitation pressure gradient (TRPG). The pulmonary vein-to-right pulmonary artery ratio (PV/PA) recently has been described for the detection of pulmonary venous congestion. Whether this variable could be used to detect the presence of precapillary PH is unknown. The objective of the present study was to investigate the diagnostic value of PV/PA for prediction of TRPG, as a surrogate of PAP, in dogs with PH of precapillary origin.

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*Animals:* Sixty-seven client-owned dogs were included in the study.
*Methods:* This was a retrospective study. Dogs with a measurable TRPG were included and classified into group 1 (TRPG $<$ 30 mmHg), group 2 (TRPG 30—49 mmHg), group 3 (TRPG 50—80 mmHg), or group 4 (TRPG $>$ 80 mmHg). The PV/PA, acceleration time-to-ejection time ratio of pulmonary artery flow, main pulmonary artery diameter-to-aortic diameter ratio, and right pulmonary artery distensibility index were measured retrospectively from cineloops in each dog.
*Results:* The PV/PA measured by both two-dimensional (2D) and time-motion mode(MM) echocardiography decreased proportionally with PH severity. Using regression analysis, PV/PA (2D) was identified as the strongest predictor for TRPG ($R^2 = 0.70$, $p < 0.0001$) among other variables studied, with a good diagnostic accuracy (area under the curve = 0.94) for moderate PH (TRPG $>$ 50 mmHg) using a cutoff value of $<$ 0.70 (sensitivity = 96%, specificity = 82%).
*Conclusions:* Results of the present study suggest that PV/PA can be useful as an additional, non-invasive, and indirect variable to identify precapillary PH in dogs.


**Abbreviations Table**

| | |
|---|---|
| 2D | two-dimensional mode |
| Ao | Aortic diameter |
| AT:ET | acceleration time-to-ejection time ratio of the pulmonary outflow |
| MM | time-motion mode |
| MPA | main pulmonary artery |
| MPA/Ao | main pulmonary artery diameter-to-aortic diameter ratio |
| PA | pulmonary artery |
| PAP | pulmonary arterial pressure |
| PH | pulmonary hypertension |
| PV | pulmonary vein |
| PV/PA | pulmonary vein-to-right pulmonary artery ratio |
| RPAD Index | Right Pulmonary Artery Distensibility Index |
| TR | tricuspid regurgitant |
| TRPG | peak tricuspid regurgitation systolic pressure gradient |

## Introduction

Pulmonary hypertension (PH) is a frequently encountered comorbid condition in dogs suffering from parasitic diseases (e.g. dirofilariasis, angiostrongylosis), thromboembolic diseases, chronic respiratory diseases (e.g. pulmonary fibrosis, chronic bronchitis), myxomatous mitral valve disease, and congenital cardiac shunts [1]. Medical treatment of PH with sildenafil may delay disease progression [2] and improve clinical signs and quality of life in dogs with PH secondary to cardiopulmonary diseases [3—5]. Diagnosis of PH in veterinary medicine relies on Doppler echocardiography for estimation of pulmonary arterial pressure (PAP) in the presence of tricuspid or pulmonic regurgitation through application of the simplified Bernoulli equation [6]. However, these measurements can be unobtainable or inaccurate when tricuspid regurgitation (TR) is absent or there is poor Doppler alignment to flow [7—9]. Those diagnostic constraints enhance the need to develop new, reliable, non-invasive surrogates for the detection of PH.

A novel echocardiographic index, the pulmonary vein-to-right pulmonary artery ratio (PV/PA), was recently described in healthy dogs [10] and has proven useful in the detection of congestive heart failure in dogs affected with degenerative mitral valve disease [11]. Whether this echocardiographic variable can indicate the presence of precapillary PH is unknown.

We hypothesized that the PV/PA would decrease proportionally to PH severity in dogs with precapillary PH and might predict Doppler-derived estimates of systolic PAP obtained from peak tricuspid regurgitation systolic pressure gradient (TRPG) with a diagnostic accuracy similar to other indirect echocardiographic variables of PH described in the literature. The study objectives were thus to assess the diagnostic value of PV/PA for prediction of TRPG in dogs with various degrees of PH and to compare this index to the acceleration time-to-ejection time ratio of the pulmonary artery flow (AT:ET) [12], the main pulmonary artery diameter-to-aortic diameter ratio (MPA/Ao)

[13], and the Right Pulmonary Artery Distensibility Index (RPAD Index) [14—16].

## Animals, materials, and methods

### Dogs

Medical records from the teaching small animal veterinary clinic of the University of Liège were reviewed for canine patients that underwent an echocardiographic study as part of a routine clinical workup between September 2011 and September 2017. Dogs with a systolic TR jet on color and continuous-wave Doppler echocardiography were included if PV/PA was recorded from either two-dimensional (2D) or time-motion mode(MM) echocardiography and if the final echocardiographic diagnosis was either 'normal cardiac examination' or 'PH of precapillary origin.' Included dogs were subdivided into four groups according to Doppler echocardiographic evidence of PH: group 1 (control group, TRPG $<$ 30 mmHg), group 2 (mild PH, TRPG of 30—49 mmHg), group 3 (moderate PH, TRPG of 50—75 mmHg), and group 4 (severe PH, TRPG $>$ 75 mmHg) [1]. Dogs with a concomitant left- or right-sided cardiac disease were excluded, with the exception of dogs with mild mitral valve disease having an end-systolic left atrium to aorta ratio $<$1.4 by 2D short-axis imaging [17].

### Echocardiographic examination

Transthoracic 2D echocardiography, MM echocardiography, and conventional Doppler echocardiography were performed by three trained observers, two board-certified veterinary cardiologists (K.M.E. and A-.C.M.), and one cardiology assistant under the direct supervision of a board-certified veterinary cardiologist, using an ultrasound unite[e] equipped with 2.2—3.5 and 5.5—7.5 MHz phased-array transducers. Dogs were placed in right and left lateral recumbency, and a simultaneous one-lead echocardiogram (ECG) was recorded. Standard right parasternal (long and short axis) and left apical parasternal views were used for data acquisition. All measurements were performed off-line by a single trained investigator (K.M.E.). The value of each echocardiographic variable studied consisted of an average of at least three representative measurements, except for pulmonary regurgitation (PR) and TR velocities for which the highest value recorded was used. A right parasternal long axis four-chamber view was optimized to simultaneously visualize the right ostium of the pulmonary veins (PV) in the longitudinal section and the right pulmonary artery (PA) in the cross section [10]. Measurements of PV and PA diameters were taken using MM and 2D imaging, as previously described, to calculate the ratios [11]. Dimensions of both vessels were obtained by tracing a line perpendicular to the medial PV and passing through the center of the adjacent right PA. For both measurements, the inner edge-to-inner edge method was used with measurements timed to the end of the T wave (end-systole). Fig. 1 illustrates 2D and MM images of PV and PA obtained in dogs with a TRPG $<$ 30 mmHg and dogs with a TRPG $>$ 50 mmHg. The right PA diameter was also measured at the end of the Q wave (end-diastole) in MM to calculate the RPAD Index following the formula: [(systolic diameter — diastolic diameter)/systolic diameter] [15]. Main pulmonary artery (MPA) diameter was measured in 2D from the right parasternal short axis view optimized on the MPA [13], and the aortic diameter (Ao) was measured at the level of the annulus [18] to calculate the MPA/Ao. The Ao also served to calculate PV/Ao and PA/Ao ratios to normalize PV and PA vessel size among individuals as PV and PA are weight-dependent variables [11]. Pulmonary outflow was recorded from the heart base view with the pulsed-wave Doppler sample positioned centrally in the flow stream between the opened pulmonic valve leaflets. The acceleration time and ejection time were measured to calculate the AT:ET ratio [12]. A similar technique was used to record PR using continuous-wave Doppler and measure peak PR pressure gradient, corresponding to mean PAP. Peak systolic TR jet velocity was measured using continuous-wave Doppler from the view that allowed the best alignment to calculate TRPG.

### Statistical analysis

Statistical analyses were performed using commercially available software[f,g]. Continuous variables were reported as median and range (minimum and maximum), and categorical data as proportions. The Shapiro-Wilk test was applied to assess the normality of distribution of continuous variables. Differences in continuous variables among groups were determined using one-way

[e] Vivid I, General Electric Medical System.

[f] XLstat software, Addinsoft SARL, Paris, France.
[g] SAS 9.3, SAS Institute, Tervueren, Belgium.

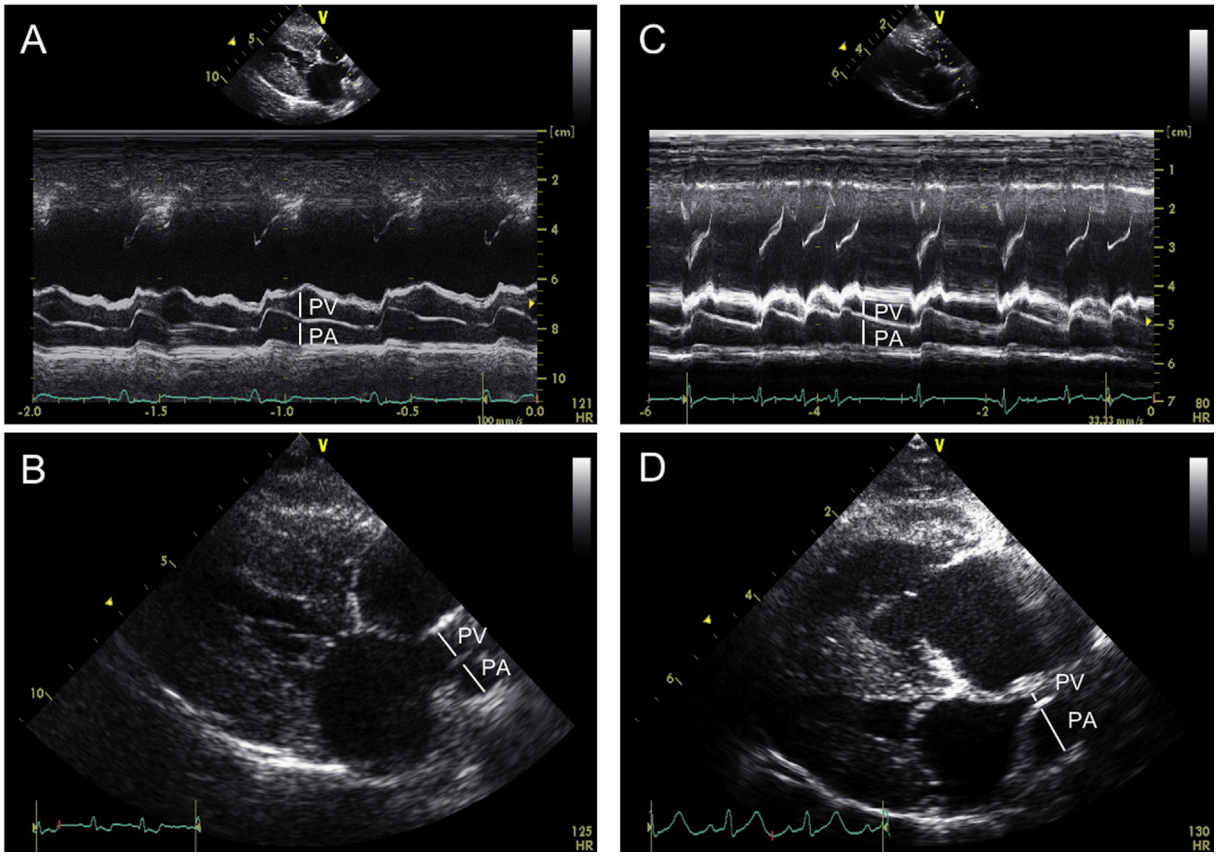


**Fig. 1** Representative measurement and calculation of the right pulmonary vein-to-pulmonary artery ratio (PV/PA) in two-dimensional (2D) and time-motion mode(MM) echocardiography. (A) PV/PA (2D) obtained in a dog with a peak tricuspid regurgitation systolic pressure gradient (TRPG) $<$ 30 mmHg; (B) PV/PA (MM) in a dog with TRPG $<$ 30 mmHg; (C) PV/PA (2D) in a dog with TRPG $>$ 50 mmHg; (D) PV/PA (MM) obtained in a dog with TRPG $>$ 75 mmHg. PA: pulmonary artery; PV: pulmonary vein.

analysis of variance (for normally distributed variables) or the Kruskal-Wallis test (for variables that were not normally distributed). When significant differences were identified, post hoc pairwise comparisons were performed using either Tukey multiple comparisons test or Dunn's test with Bonferroni corrections (for non-normal data). Results of statistical procedures with regard to PV/PA were also depicted graphically by means of scatterplots. Proportions were compared using Fisher exact test. Simple linear regression between TRPG values and the echocardiographic variables studied (PV/PA, AT/ET, MPA/Ao, RPAD Index) was performed. To identify the best one-variable model, an all-subsets regression analysis was performed with a maximum $R^2$ improvement as the selection criterion. Receiver operator characteristic (ROC) curve analyses were performed to determine optimal cutoff values of PV/PA, RPAD index, AT:ET, and MPA/Ao for the prediction of TRPG $>$50 mmHg. For all analyses, $p \leq 0.05$ was considered statistically significant.

## Results

### Dogs

Detailed features of the study sample according to subgroup division are summarized in Table 1. Sixty-seven dogs were included in the study: 21 dogs served as controls (group 1), 17 dogs had mild PH (group 2), 12 dogs had moderate PH (group 3), and 17 dogs had severe PH (group 4). None of the dogs had any arrhythmia other than sinus arrhythmia. Eight dogs had evidence of mild degenerative mitral valve disease with normal left atrial and ventricular dimensions. Six dogs were mixed breeds; five were Yorkshire terriers; four each were Maltese, Chihuahuas, and Jack Russell terriers; three each were border collies, French bulldogs, pugs, Labrador retrievers, Shetland sheepdogs, shih tzus, and dachshunds; and two each were Belgian shepherds and West Highland white terriers. The other breeds (German

**Table 1** Characteristics of study sample.

| Variables | Control dogs TRPG <30 mmHg (group 1) | Mild PH TRPG 30–49 mmHg (group 2) | Moderate PH TRPG 50–75 mmHg (group 3) | Severe PH TRPG >75 mmHg (group 4) | Overall *p*-value |
|---|---|---|---|---|---|
| TR, n | 21 | 17 | 12 | 17 | n.a. |
| TRPG (mmHg) | 16.9 (3.4–29.4) | 39.9 (31.4–49.0) | 67.4 (56.0–75.3) | 107.4 (82.4–157.8) | n.a. |
| Sex (F/M) | 10/11 | 11/6 | 7/5 | 9/8 | 0.749 |
| Age (years) | 5.2 (0.4–14.9) | 7.2 (1.0–14.8) | 10.4 (0.9–13.8) | 6.4 (0.6–15.5) | 0.100 |
| BW (kg) | 16.0 (3.6–41.0) | 8.0 (2.7–33.0) | 8.0 (2.8–40.0) | 7.4 (2.3–38.4) | 0.062 |
| PR, n | 3 | 2 | 6 | 9[a,b] | 0.009 |
| PRPG (mmHg) | 1.0 (1.1–12.7) | 27.0 (26.2–27.9) | 27.4 (7.2–41.5) | 32.3 (8.4–55.7)[a] | 0.026 |

BW: body weight; F: female; M: male; n: sample size; PH: pulmonary hypertension; PR: pulmonary regurgitant jet; PRPG: peak pulmonary regurgitation diastolic pressure gradient; TR: tricuspid regurgitant; TRPG: peak tricuspid regurgitation systolic pressure gradient. Data are expressed as median and range (minimum – maximum).

[a] Indicates $p < 0.05$ as compared to group 1.

[b] Indicates $p < 0.05$ as compared to group 2.

shepherd, Switzerland white shepherd, Catalan shepherd, Boston terrier, Hungarian pointer, bull terrier, cairn terrier, Collie, Brittany spaniel, Galgo, golden retriever, Belgian griffon, Havanese, Siberian husky, Pomeranian, miniature Poodle, Gordon setter, miniature spitz, and whippet) were each represented once. Eleven dogs were clinically healthy. The remaining 56 dogs were suffering from angiostrongylosis (n = 22), bronchomalacia (n = 10), precapillary PH of unknown origin (n = 8), brachycephalic syndrome (n = 6), pulmonary thromboembolism (n = 5), heartworm disease (n = 2), eosinophilic bronchopneumopathy (n = 1), pulmonary fibrosis (n = 1), or diffuse pulmonary carcinoma (n = 1).

No statistical difference in age, body weight, and gender repartition was noted between the four study groups. Pulmonary valve regurgitation was measured in a higher proportion of dogs in group 4 than in groups 1 and 2, with significantly higher peak PR diastolic pressure gradient in group 4 than in group 1 (Table 1). At the time of echocardiographic examination, 15 dogs were treated with antibiotics, 14 with steroids, nine dogs with pimobendan, six dogs with ACE-inhibitors, ten dogs with diuretics, seven dogs with sildenafil, five dogs with clopidogrel, and five dogs with theophylline. Twenty-nine dogs were untreated.

## Echocardiographic results

Echocardiographic data are presented in Table 2. The PV/PA measured by 2D and MM echocardiography proportionally decreased with increasing PH severity (Fig. 2). This decrease resulted from an increase in PA size and also from a decrease in PV size, as displayed by PA/Ao and PV/Ao changes in both imaging modes (Table 2). A decrease in RPAD Index and AT:ET as well as an increase in MPA/Ao variables were also noted with regard to PH severity (Table 2).

## Regressions and ROC curve analyses

Results of simple regression analyses are shown in Table 3. The selection of the best one-variable model reported that PV/PA (2D) was the strongest predictor for TRPG with an $R^2$ of 0.70 ($p < 0.001$, n = 41). Receiver operating characteristic curves for each echocardiographic variable for the prediction of TRPG > 50 mmHg are presented in Fig. 3. Pulmonary vein-to-right pulmonary artery ratio (2D) and RPAD Index demonstrated the greatest area under the curve for TRPG prediction. Three cutoff values were determined from the ROC analyses for each echocardiographic variable studied. Table 4 summarizes the cutoffs with the optimal test efficiency (highest Youden index), the maximum sensitivity, and the maximal specificity for predicting TRPG > 50 mm Hg.

## Discussion

Assessment of PH can be challenging in veterinary medicine. Doppler estimation of PAP via the measurement of TRPG is not always feasible or accurate [8], and catheterization of the right heart is not routinely performed because of cost and invasiveness of the procedure. In the present investigation, we evaluated the performance of the calculated variable, PV/PA, as a non-invasive and indirect echocardiographic predictor for the

**Table 2** Echocardiographic results of all study dogs (n = 67).

| Echocardiographic variables | Control dogs TRPG <30 mmHg (group 1) n = 21 | Mild PH TRPG 30–49 mmHg (group 2) n = 17 | Moderate PH TRPG 50–75 mmHg (group 3) n = 12 | Severe PH TRPG > 75 mmHg (group 4) n = 17 | Overall *p*-value |
|---|---|---|---|---|---|
| PV/PA (MM) | 1.000 (0.743–1.290) (n = 21) | 0.639[a] (0.333–1.232) (n = 15) | 0.508[a] (0.258–0.756) (n = 10) | 0.369[a,b] (0.222–0.726) (n = 16) | <0.0001 |
| PV/PA (2D) | 0.958 (0.696–1.060) (n = 20) | 0.771 (0.378–1.144) (n = 13) | 0.482[a] (0.204–0.722) (n = 12) | 0.371[a,b] (0.193–0.625) (n = 15) | <0.0001 |
| PV/Ao (MM) | 0.477 (0.356–0.680) (n = 21) | 0.362[a] (0.219–0.602) (n = 15) | 0.397[a] (0.176–0.567) (n = 10) | 0.330[a] (0.186–0.438) (n = 16) | 0.001 |
| PA/Ao (MM) | 0.479 (0.349–0.620) (n = 21) | 0.588 (0.448–0.735) (n = 15) | 0.656[a] (0.554–0.803) (n = 10) | 0.806[a,b] (0.541–1.108) (n = 16) | <0.0001 |
| PV/Ao (2D) | 0.423 (0.309–0.619) (n = 20) | 0.344 (0.204–0.592) (n = 13) | 0.332 (0.127–0.488) (n = 12) | 0.238[a] (0.154–0.408) (n = 15) | 0.007 |
| PA/Ao (2D) | 0.433 (0.324–0.595) (n = 20) | 0.541 (0.332–0.689) (n = 13) | 0.660[a,b] (0.515–0.815) (n = 12) | 0.755[a,b] (0.568–1.078) (n = 15) | <0.0001 |
| RPAD Index, % | 38.8 (22.3–47.0) (n = 19) | 28.8 (20.4–55.4) (n = 12) | 19.9[a] (9.1–31.4) (n = 9) | 8.9[a,b] (0.0–27.4) (n = 15) | <0.0001 |
| AT:ET | 0.494 (0.253–0.627) (n = 20) | 0.448 (0.230–0.539) (n = 17) | 0.318[a,b] (0.265–0.390) (n = 11) | 0.329[a,b] (0.169–0.494) (n = 14) | <0.0001 |
| MPA/Ao | 0.809 (0.599–0.888) (n = 17) | 0.847 (0.695–1.094) (n = 15) | 0.824 (0.757–1.106) (n = 9) | 1.145[a,b] (0.907–1.396) (n = 13) | 0.005 |

2D: two-dimensional mode; AT:ET: acceleration time-to-ejection time ratio of the pulmonary flow; MM: time-motion mode; MPA/Ao: main pulmonary artery-to-aorta diameters ratio; PA/Ao: pulmonary artery-to-aortic diameters ratio; PH: pulmonary hypertension; PV/Ao: right pulmonary vein-to-aortic diameters ratio; PV/PA: right pulmonary vein-to-pulmonary artery diameters ratio; RPAD Index: right pulmonary artery distensibility index; TRPG: peak tricuspid regurgitation systolic pressure gradient. Data are expressed as median and range (minimum – maximum).

[a] Indicates $p < 0.05$ as compared to group 1.

[b] Indicates $p < 0.05$ as compared to group 2.

diagnosis of precapillary PH in a clinical setting. We demonstrated that PV/PA proportionally decreased with increasing PH severity in dogs affected with precapillary PH. Among the echocardiographic variables studied, PV/PA (2D) was the strongest predictor for TRPG with a good diagnostic accuracy for moderate PH (TRPG > 50 mmHg). These findings support the use of PV/PA when screening dogs for precapillary PH via echocardiography.

Birettoni et al (2010)[h] first described the use of the PV/PA in dogs at the 20th ECVIM Congress. Thereafter, two studies reported reference intervals in healthy dogs with a mean PV/PA of 1 in both 2D and MM and a good intraobserver and interobserver reproducibility [10,11]. In the present study, a median PV/PA value around 1 was again found in control dogs and significantly lower PV/PA values in dogs with precapillary PH in proportion with PH severity. The reduced PV/PA was attributable to both an increase in PA size and a decrease in PV size, as informed by changes in PV/Ao and PA/Ao between the groups. Pulmonary artery distension in dogs with PH might be explained by an increased pulmonary vascular bed resistance secondary to the underlying disease. Decreased PV diameter can be speculated to stem from reduction of left ventricular preload secondary to increased pulmonary arterial resistance,

[h] Birettoni F, Caivano D, Giorgi ME, Rishniw M, Moise S, Porciello F. A novel echocardiographic index in the dog: pulmonary vein:pulmonary artery diameter. The 20th annual ECVIM congress. Toulouse, France, 2010.

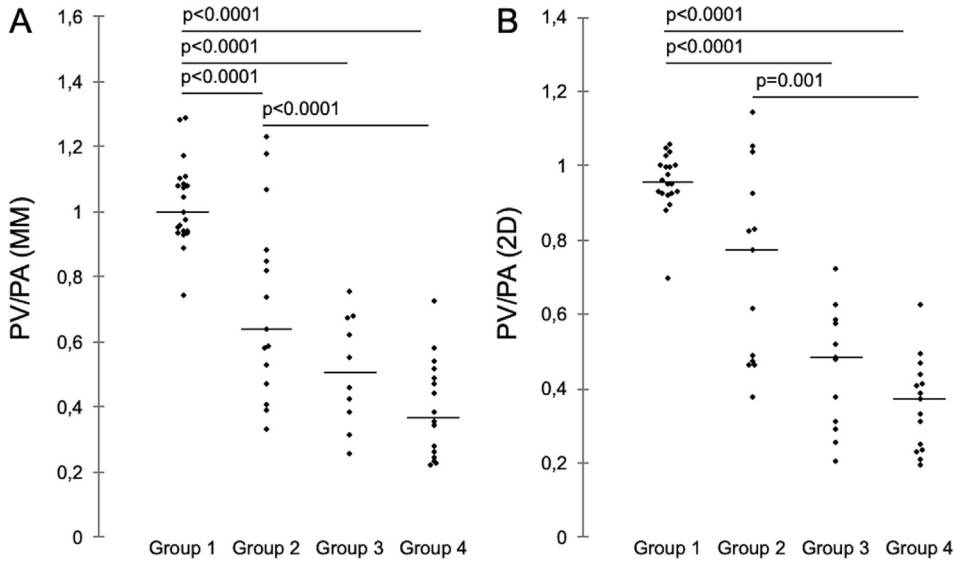


**Fig. 2** Scatterplots illustrating right pulmonary vein-to-pulmonary artery (PV/PA) values in both time-motion mode(MM) (A) and two-dimensional (2D) mode (B) obtained in control dogs with a peak tricuspid regurgitation systolic pressure gradient (TRPG) < 30 mmHg (group 1) and in dogs suffering from mild pulmonary hypertension (PH) (TRPG 30—49 mmHg, group 2), moderate PH (TRPG 50—75 mmHg, group 3), and severe PH (TRPG > 75 mmHg, group 4). Median is indicated by the horizontal line.

from decreased right ventricular function, from compression of the vein by the enlarged adjacent artery, or some combination of these factors. Diuretic administration also could have contributed to decreased preload in some dogs. Many of these canine patients were receiving diuretics or other treatments for clinical signs of disease, and therapy was uncontrolled in this retrospective study.

Doppler-derived systolic time intervals of pulmonary outflow (AT:ET), MPA/Ao, and RPAD Index have all been described as indirect predictors of PH in dogs [12—16] and were again measured in the present study. A significant increase of MPA/Ao and decrease of RPAD index and AT/ET were found in proportion with PH severity, which supports previously published veterinary studies [12—16]. Among all the echocardiographic variables studied, PV/PA (2D) was the strongest predictor for TRPG with a coefficient of determination of $R^2 = 0.70$. Receiver operating characteristic curve analyses revealed that PV/PA (2D) had a diagnostic accuracy as good as RPAD index and better than MPA/Ao and AT:ET for the diagnosis of moderate PH (TRPG > 50 mmHg). This is a clinically relevant finding. There are additional advantages of PV/PA for detection of PH. A simple and reproducible variable requires minimal training to acquire and can be obtained by routine 2D or MM echocardiography and from a single frame [11]. As with RPAD index, these linear measurements are not hampered by Doppler alignment limitations. Cut-off values obtained for the prediction of TRPG >50 mmHg using MPA/Ao, AT:ET, and RPAD index

**Table 3** Results of simple regression analyses for the prediction of TRPG.

| Variable | n | $R^2$ | *p* | Regression equation |
|---|---|---|---|---|
| PV/PA (MM) | 62 | 0.60 | <0.0001 | TRPG = 120.53—94.31 * PV/PA (MM) |
| PV/PA (2D) | 60 | 0.68 | <0.0001 | TRPG = 120.37—101.69 * PV/PA (2D) |
| RPAD Index | 55 | 0.56 | <0.0001 | TRPG = 112.51—2.26 * RPAD |
| AT:ET | 62 | 0.33 | <0.0001 | TRPG = 131.16—197.37 * ATET |
| MPA/Ao | 54 | 0.52 | <0.0001 | TRPG = −86.62 + 158.11 * MPA/Ao |

2D: bi-dimensional mode; AT:ET: acceleration time-to-ejection time ratio of the pulmonary flow; MM: time-motion mode; MPA/Ao: main pulmonary artery-to-aorta diameters ratio; n: sample size; PV/PA: right pulmonary vein-to-pulmonary artery ratio; $R^2$: coefficient of determination; RPAD Index: right pulmonary artery distensibility index; TRPG: peak tricuspid regurgitation systolic pressure gradient.

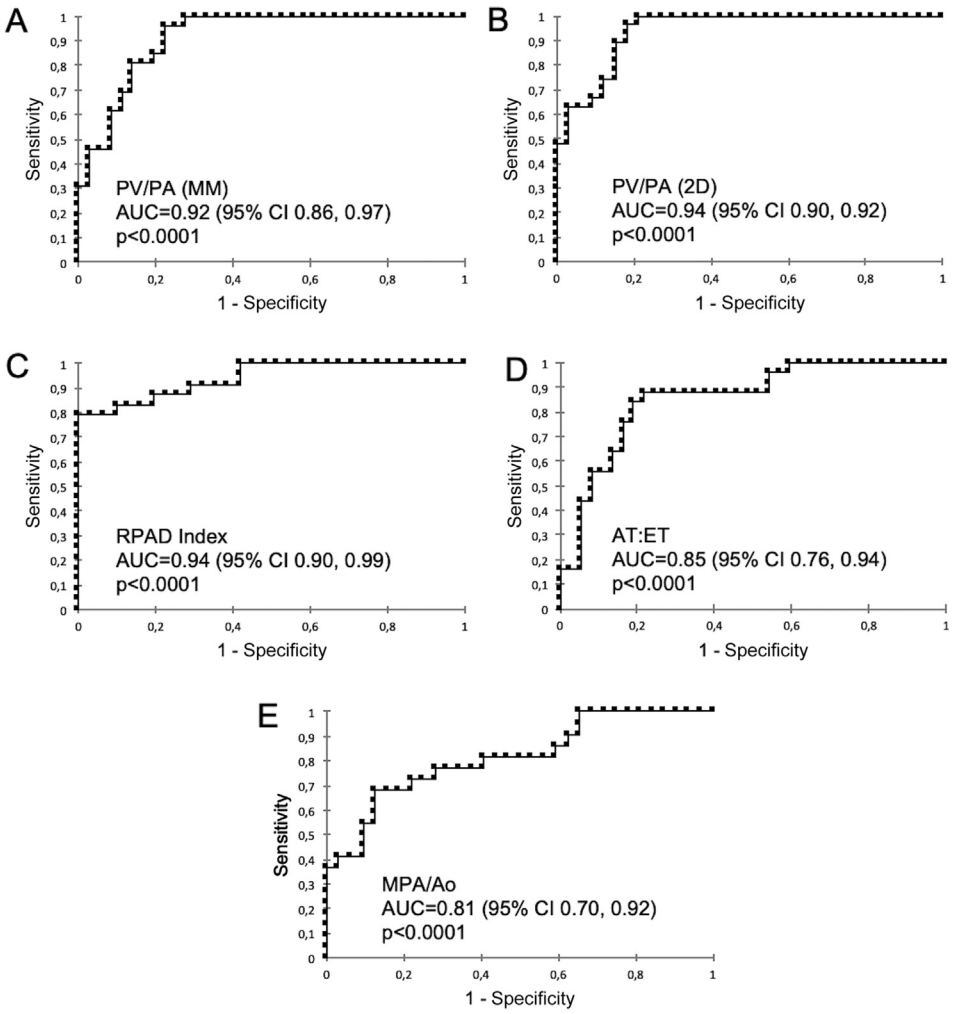


**Fig. 3** Receiver operating characteristic curves of indirect echocardiographic variables of pulmonary hypertension: right pulmonary vein-to-pulmonary artery (PV/PA) in both MM (A) and 2D (B), Right Pulmonary Artery Distensibility Index (RPAD Index) (C), acceleration time-to-ejection time ratio of the pulmonary outflow (AT:ET) (D), and main pulmonary artery-to-aorta diameters ratio (MPA/Ao) (E) for the prediction of peak tricuspid regurgitation systolic pressure gradient (TRPG) $>$ 50 mmHg. AUC: area under the curve; CI: confidence interval.

were slightly different than those reported in previous studies. This might be explained by the use of different thresholds to define a TRPG suggestive of PH and by the heterogeneity of studies population. Dogs included in the present study were suffering from a variety of diseases, mostly angiostrongylosis (32.8% of included dogs), a disorder associated with the development of precapillary PH; conversely, dogs in other studies were suffering from other diseases associated with precapillary, postcapillary, or mixed causes of PH [12—14].

The main limitation of the present study was that PAPs were not directly measured by right heart catheterization. This technique was not chosen because it is invasive, has inherent risk of complications, and would have required heavy sedation or general anesthesia. Typical of clinical practice, we used Doppler echocardiography—derived estimates of PAP (TRPG) as a surrogate measure of PAP, accepting that relevant differences have been reported between TRPG-estimated and invasively measured PAP [8]. This limitation should be kept in mind when classifying the severity of PH in dogs using the cutoff values presented herein. A second limitation of this retrospective study was that not all variables were measurable in all dogs. Moreover, treatments were uncontrolled and some of the dogs were receiving cardiac or vasoactive drug therapies at the time of echocardiography. This could have confounded or biased the measurements or their interpretation. Different therapies were nearly equally distributed across the groups, which might have mitigated the

**Table 4** Sensitivity (Se), specificity (Sp), and Youden index (Y index) of different cutoff points of indirect echocardiographic parameters of PH for prediction of peak tricuspid regurgitation systolic pressure gradient (TRPG) > 50 mmHg.

| Variable | AUC | 95% CI | *p* | Cutoff | Se | Sp | Y Index |
|---|---|---|---|---|---|---|---|
| PV/PA (MM) | 0.92 | 0.86, 0.97 | <0.0001 | <0.82 | 1.00 | 0.72 | 0.84 |
| | | | | **< 0.74** | **0.96** | **0.78** | **0.85** |
| | | | | <0.33 | 0.31 | 1.00 | 0.71 |
| PV/PA (2D) | 0.94 | 0.90, 0.92 | <0.0001 | <0.77 | 1.00 | 0.79 | 0.88 |
| | | | | **< 0.70** | **0.96** | **0.82** | **0.88** |
| | | | | <0.38 | 0.48 | 1.00 | 0.77 |
| RPAD Index, % | 0.94 | 0.90, 0.99 | <0.0001 | <31.5 | 1.00 | 0.58 | 0.76 |
| | | | | **< 20.4** | **0.79** | **1.00** | **0.91** |
| | | | | <20.4 | 0.79 | 1.00 | 0.91 |
| AT:ET | 0.85 | 0.76, 0.94 | <0.0001 | <0.50 | 1.00 | 0.41 | 0.65 |
| | | | | **< 0.42** | **0.88** | **0.78** | **0.82** |
| | | | | <0.23 | 0.16 | 1.00 | 0.66 |
| MPA/Ao | 0.81 | 0.70, 0.92 | <0.0001 | >0.75 | 1.00 | 0.34 | 0.61 |
| | | | | **> 0.93** | **0.68** | **0.87** | **0.80** |
| | | | | >1.09 | 0.36 | 1.00 | 0.74 |

2D: two-dimensional mode; AT:ET: acceleration time-to-ejection time ratio of the pulmonary flow; AUC: area under receiver operating characteristic curve; CI: confidence interval; MM: time-motion mode; MPA/Ao: main pulmonary artery-to-aorta diameters ratio; PH: pulmonary hypertension; PV/PA: right pulmonary vein-to-pulmonary artery ratio; RPAD Index: right pulmonary artery distensibility index; Se: sensitivity; Sp: specificity.
Bold values represent a clinically relevant cutoff, with the least amount of overlap between groups.

impact of treatments on the statistical results. Another study limitation was that the cardiologist who performed cardiac measurements was not blinded to the degree of PH, thus potentially biasing the results.

## Conclusions

Results of the present study highlight the potential usefulness of echocardiographically derived PV/PA as a complementary, non-invasive tool for the diagnosis of at least moderate, precapillary PH determination in dogs. This variable should be particularly useful when TR is absent or difficult to measure. Further studies are needed to determine the utility of PV/PA in the diagnosis of mixed or postcapillary PH and for monitoring the effects of therapy on PH.

## Conflict of Interest Statement

The authors do not have any conflicts of interest to disclose.

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## Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jvc.2019.06.001.

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